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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/846,687	05/01/2001	Lorrence H. Green		2915

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06/20/2005

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EXAMINER

BROWN, TIMOTHY M

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/846,687

Applicant(s)

GREEN, LORRENCE H.

Examiner

Timothy M. Brown

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2001 and 10 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) 6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 7-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

S.O.O.

DETAILED ACTION

This non-final Office action is responsive to the communication received October 1, 2004. Claims 1-10 are pending. Claims 1-5 and 7-10 are under examination, while claim 6 is withdrawn.

Election

Applicant's election of Group II, *without traverse*, in the communication received October 1, 2004 is acknowledged. Applicant's election is without traverse because Applicant did not particularly point out any alleged errors in the restriction requirement.

Specification

The specification is objected to for being ungrammatical in that it recites "demonstrated in the case of . . ." on page 10, line 9.

Claim Objections

Claims 1, 4, 6 and 8 are objected to for failing to refer to the claimed polypeptide by its sequence number.

35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-5 and 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in that it lacks antecedent basis for the limitation "the body" in line 1.

Claims 1 and 4 are indefinite in the recitation of "the region of the CCR5 receptor in wild-type individuals, that is affected by the delta 32 deletion" This language does not define whether the claimed region comprises (1) the CCR5 32 base-pair deletion itself, or (2) a region of the CCR5 protein that interacts with (i.e. is affected by) the region that makes up the 32-base pair deletion.

Claims 1 and 4 are indefinite in the recitation of "using a vaccine" in that it is unclear, even in light of the specification, what the step of using involves. As claimed, "using a vaccine" may refer to administering a vaccine to the patient, or using the vaccine to produce antibodies to be used in passive immunotherapy. The scope of claims 1 and 4 is therefore indefinite.

Claims 3 and 10 are indefinite in the recitation of "said vaccine produces an antibody bound to the CCR5 site." This language does not specify to one skilled in the art whether the vaccine produces (1) a translation product that is a heterodimer of CCR5 and an anti-CCR5 antibody, or (2) an antibody with specificity for the CCR5 receptor.

Claim 3 is indefinite in that the limitation "the CCR5 site" lacks antecedent basis.

Claim 7 is indefinite in the recitation of "providing a polypeptide" in that this step does not make it clear that the claimed "method of vaccination" administers a polypeptide to an individual; claim 7 lacks the recitation of an individual. The scope of claim 7 is therefore indefinite.

Claim 7 is indefinite in the recitation of "inactivating viral receptors." This language fails to indicate whether "inactivating" refers to binding and opsonizing the viral receptors, or inhibiting the activity of the receptors through competitive binding.

35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 7-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Undue experimentation is defined by the following factors: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation

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needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

The breadth of Applicant's claims provide for a method of treating HIV infection through the administration of a polypeptide vaccine comprising a region of the CCR5 receptor. Thus, the nature of the invention is a method for treating HIV infection by inducing the body to produce self-antibodies that interfere with the binding of virus to the CCR5 receptor.

Although the level of skill in the HIV vaccine art was high at the time of Applicant's invention, the state of the art had not witnessed an HIV therapy based on self-antibodies against the CCR5 receptor. At the time of Applicant's invention, it was just being discovered that a small fraction of HIV-resistant individuals produced self antibodies against the CCR5 receptor. *J. Immun.* (March 2000) 164, 6, 3426-3433; *Hum. Immun.* (2001) 62, 143-145. Thus, the state of the art at the time of Applicant's invention merely suggested that anti-CCR5 antibody may be involved in HIV resistance. Moreover, producing a vaccine that induces the production of self-antibodies against the CCR5 receptor was an unpredictable method for treating HIV. This results because inducing the body to produce antibodies against syngeneic antigens was fraught with difficulty. This is partly due to the fact that naïve B-cells that recognize self antigens are destroyed by the immune system during lymphocyte maturation. *Immunobiology*, 5th ed. (2001). Due to the unpredictability of inducing an immune response against the CCR5 self-antigen, one skilled in the art would have to rely heavily on Applicant's specification in order to reduce the claimed invention to practice. However, the content

of Applicant's specification does not teach how to induce self-antibodies against a syngeneic antigen. The specification instead consists of a Detailed Specification having only three pages which mainly refer to the substitutions that can be made to obtain derivatives of the claimed polypeptide. There is no disclosure of how to induce antibodies against a syngeneic antigen such as the claimed polypeptide. Applicant's failure to provide working examples, of any kind, also contributes to the specification's lack of guidance. Thus, one skilled in the art would not know what dosage of the vaccine to administer, what adjuvants and/or administration schedules to follow, or what route of administration to use in order to prevent infection. It is also worth noting that the results that are referred to are prophetic in that the specification provides, for example, that the claimed compound "will also prevent early active infections . . ." (page 12). Thus, the specification lacks the guidance of working examples.

Research five years after Applicant's filing date indicates that inducing an immune response against a syngeneic CCR5 polypeptide is truly involved. Barassi et al. showed that producing antibodies in this manner at least requires engineering a chimeric CCR5 polypeptide that has precise conformational constraints (J. Virol. (June 2005) 79, No. 11, 6848-6858). Current research therefore provides further evidence that at the time the application was filed, Applicant's limited specification failed to provide adequate guidance as to how one skilled in the art might induce self-antibodies against a syngeneic CCR5 polypeptide.

Based on the foregoing, Applicant's specification would require one skilled in the art to invest undue experimentation in order to practice the claimed invention.

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Claims 4 and 5 further lack enablement in that the specification fails to teach, without undue experimentation, "a method of treating a patient infected with HIV"

Claim 4 is broadly drawn to a method of preventing the spread of HIV in a patient by administering a vaccine that comprises a polypeptide from the CCR5 receptor. At the time the application was filed, the vaccine art had not witnessed an anti-CCR5 vaccine, let alone one capable of preventing the spread of HIV. Research indicates that reducing such a vaccine to practice was truly unpredictable. Zuber et al. showed that although some immune response against a syngeneic CCR5 could be achieved, getting the antibody to prevent the spread of infection was problematic (Virology (December 2000) 278, 400-411). Moreover, decreasing the spread of infection could not be accomplished for some strains. Research by Barassi et al. further demonstrates that the efficacy of CCR5 vaccines was unpredictable. Their research showed that although CCR5 vaccines can limit infection by downregulating CCR5 expression, this effect is only transitory. This results because the possibility of later infection still existed since the vaccine only down-regulated CCR5 expression and left some receptor available for binding virus (J. Virol. (June 2005) 79, 11, 6848-6958). Given this unpredictability, one skilled in the art would have to rely heavily on the specification in order to practice the claimed invention without investing undue experimentation. However, the content of the specification provides little guidance as to how to prevent the spread of infection using a CCR5 polypeptide vaccine. Applicant's "Detailed Specification" contains only three pages of disclosure. These three pages fail to detail how one skilled in the art might induce an immune response against a syngeneic antigen. The pages also fail to detail

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how one skilled in the art might achieve a long-term induction of antibodies that are capable of preventing the infection of the various forms of HIV. It is also worth noting the specification lacks the guidance of working examples. Thus, there is no data to teach one skilled in the art the dosages, schedules, and/or antigenic constituents that would produce a long-term expression of anti-CCR5 antibody that is capable of preventing the spread of infection. Based on this lack of disclosure, one skilled in the art would have to invest undue experimentation in order to practice the invention of claims 4 and 5.

Claims 2, 5 and 7-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2, 5 and 9 lack adequate written description for “the derivatives” of the claimed polypeptide. Given the breadth of this language, the claimed polypeptide can be made into a derivative through any number of modifications. The specification provides that a derivative of the claimed polypeptide may be obtained through a number of substitutions, methylation, hydration, or “other standard chemical methods” (Specification, p. 12). However, the specification does not teach those regions of the claimed polypeptide that are critical to the polypeptide’s antigenicity. It is clear that the immunogenicity of a peptide may be destroyed through minor changes. Thus, obtaining a derivative of the claimed polypeptide would require a knowledge of those regions that

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are responsible for the polypeptide's antigenicity. Because Applicant's have not disclosed the regions that are critical to the polypeptide, the specification fails to convey to one skilled in the art that Applicant's were in possession of derivatives of the claimed polypeptide.

Claim 7 lacks written description for a method of vaccination comprising "providing a polypeptide" that induces antibodies that are capable of "inactivating viral receptors" Claim 7 lacks adequate written description for "providing a polypeptide" because Applicant's specification only discloses a single polypeptide vaccine (i.e. SEQ ID NO:1). Applicant has not disclosed the antigenic determinants that contribute to the polypeptide's immunogenicity. That is, there is no disclosure of the polypeptide's critical amino acid regions and/or conformations. Thus, the specification does not convey to one skilled in the art that Applicant was in possession of any polypeptide (i.e. derivative) beyond SEQ ID NO:1.

Claim 7 also lacks adequate written description for "inactivating viral receptors" Although the specification discloses CCR5 self-antibodies that interfere with the CCR5 receptor, it does not disclose antibodies capable of interfering with any other form of viral receptor. Viral infectivity and replication involves specific viral/cell surface protein interactions that enable the virus to bind and enter the cell. In many cases, these infectivity pathways are unknown making the identification of infectious receptor proteins even more difficult. Thus, the specification does not convey to one skilled in the art that at the time the application was filed, Applicant was in possession of anything more than using anti-CCR5 antibodies for preventing the binding of HIV.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Smith et al. (WO 92/22654).

Claim 7 is interpreted as being drawn to administering a vaccine that causes the body to produce antibodies that are capable of inactivating viral receptors. Smith et al. disclose administering a vaccine that is capable of interfering with the binding of gp120 with host ligand (see e.g. p. 2). Smith et al. therefore anticipate the subject matter of claim 7.

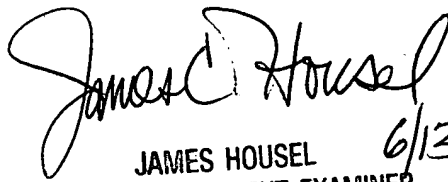
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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